(2) *Moisture.* Proceed as directed in §436.201 of this chapter.

(3) *Dissolution.* Proceed as directed in §436.541 of this chapter, except:

(i) A distance of 2.5±0.2 centimeters should be maintained between the lower edge of the stirring blade and the lowest inner surface of the vessel during test rather than 4.5±0.5 centimeters as specified in paragraph (a) of that section; and

(ii) In lieu of paragraph (d) of that section, use the interpretation described in the United States Pharmacopeia XX dissolution test.

[47 FR 11857, Mar. 19, 1982, as amended at 50 FR 19919, May 13, 1985]

§442.154 Cefpodoxime proxetil oral dosage forms.

§442.154a Cefpodoxime proxetil tablets.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefpodoxime proxetil tablets are composed of cefpodoxime proxetil and one or more suitable and harmless diluents, binders, lubricants, colorings, and coating substances. Each tablet contains cefpodoxime proxetil equivalent to either 100 milligrams or 200 milligrams of cefpodoxime. Its cefpodoxime proxetil content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of cefpodoxime that it is represented to contain. Its loss on drying is not more than 5 percent. It passes the dissolution test. It passes the identity test. The cefpodoxime proxetil used conforms to the standards prescribed by §442.54(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefpodoxime proxetil used in making the batch for potency, isomer ratio, moisture, and identity.

(B) The batch for content, loss on drying, dissolution, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The cefpodoxime proxetil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 100 tablets.

(b) *Tests and methods of assay*—(1) *Cefpodoxime content.* Proceed as directed in §442.54(b)(1), preparing the sample solution and calculating the cefpodoxime content as follows:

(i) *Preparation of sample solution.* Obtain the average tablet weight of at least 20 tablets. Grind the tablets using a mortar and pestle. Weigh approximately 660 milligrams into a suitable container. Add 30 milliliters of internal standard solution. Shake for 30 minutes using a horizontal platform shaker or equivalent. Centrifuge for about 10 minutes at 3,000 revolutions per minute until the particulate matter has settled. Withdraw a 1 milliliter aliquot of the supernatant and dilute with 9 milliliters of dilution solvent. The sample solutions are stable for at least 48 hours. Refrigeration is not recommended.

(ii) *Calculations.* Calculate the cefpodoxime content as follows:

$$\text{Milligrams of cefpodoxime per tablet} = \left(R_{sam}/R_{std}\right)\times\left(W_{std}/W_{sam}\right)\times\left(F_1/F_3\right)\times F_2\times F_4\times P$$

where:

R_{sam} = Ratio of cefpodoxime proxetil peaks area (sum of both epimers) to the internal standard peak area in the sample preparation;

R_{std} = Ratio of cefpodoxime proxetil peaks area (sum of both epimers) to the internal standard peak area in the standard preparation;

W_{std} = Weight of cefpodoxime proxetil reference standard, in milligrams;

W_{sam} = Weight of sample, in milligrams;

F_1 = Volume of internal standard used in the sample preparation, in milliliters;
F_2 = 0.766; The ratio of molecular weight for free-acid cefpodoxime over the molecular weight of cefpodoxime proxetil (427.46/557.61);
F_3 = Volume of internal standard used in the standard preparation, in milliliters;
F_4 = Average tablet weight, i.e., weight of tablets used in sample preparation divided by the number of tablets; and
P = Purity of the cefpodoxime proxetil reference standard, expressed as a decimal.

(2) *Loss on drying.* Proceed as directed in §436.200(a) of this chapter, except dry the sample at a temperature of 80° C and a pressure of 5 millimeters of mercury or less for 16 hours.

(3) *Dissolution test.* Proceed as directed in §436.215 of this chapter. The quantity Q (the amount of cefpodoxime activity dissolved) is 70 percent within 30 minutes.

(4) *Identity.* Using the high-performance liquid chromatographic procedure described in paragraph (b)(1) of this section, the retention times for the peaks of the active ingredients must be within 2 percent of the retention times for the peaks of the corresponding reference standards.

[60 FR 58232, Nov. 27, 1995]

§442.154b Cefpodoxime proxetil granules for oral suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefpodoxime proxetil granules for oral suspension is cefpodoxime proxetil and one or more suitable and harmless preservatives, sweeteners, suspending agents, buffers, and flavorings. When constituted as directed in the labeling, each milliliter contains the equivalent of either 10 or 20 milligrams cefpodoxime activity. Its cefpodoxime proxetil content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of cefpodoxime that it is represented to contain. Its loss on drying is not more than 0.5 percent. When constituted as described in the labeling, the pH of the suspension is not less than 4 and not more than 5.5. It passes the identity test. The cefpodoxime proxetil used conforms to the standards prescribed by §442.54(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefpodoxime proxetil used in making the batch for potency, isomer ratio, moisture, and identity.

(B) The batch for content, loss on drying, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The cefpodoxime proxetil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 10 intermediate containers.

(b) *Tests and methods of assay*—(1) *Cefpodoxime content.* Proceed as directed in §442.54(b)(1), preparing the sample solution and calculating the cefpodoxime content as follows:

(i) *Preparation of sample solution.* Reconstitute as directed in the labeling. Immediately before sampling the suspension, shake vigorously for several seconds. Into a suitable container, accurately weigh out 6 grams of the 50 milligrams per 5 milliliters suspension, or 3 grams of the 100 milligrams per 5 milliliters suspension. Add 5 milliliters of internal standard solution and 25 milliliters of dilution solvent. Shake for 30 minutes using a horizontal platform shaker or equivalent. Centrifuge for about 10 minutes at 3,000 revolutions per minute until the particulate matter has settled. Withdraw a 1 milliliter aliquot of the supernatant and dilute with 1 milliliter of dilution solvent. The sample solutions are stable for at least 48 hours. Refrigeration is not recommended.

(ii) *Calculations.* Calculate the cefpodoxime content as follows: